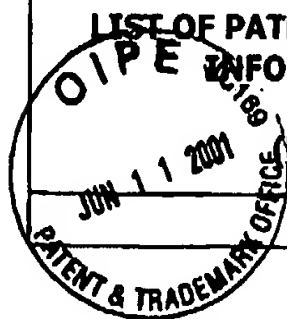


LIST OF PATENTS AND OTHER ITEMS FOR APPLICANT'S  
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METABASIS THERAPEUTICS, INC.FILING DATE:  
March 5, 1999GROUP:  
1614

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE
TM	AA	3,018,302	01.23.62	Bielefeld, et al.			
	AB	5,157,027	10/20 92	Biller, et al.			
	AC	5,658,889	8/19/97	Gruber, et al.			

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
							YES	NO
TM	AD	0 002 062 A	30.05.79	EP (Abstract)				
	AE	0 072 531 A	23.02.83	EP (Abstract)				
	AF	0 158 057 A	16.10.85	EP (Abstract)				
	AG	0 180 276	28.12.88	EP				
	AH	0 261 283	22.09.86	EP				
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	AL	0 481 214 A	22.04.92	EPO				
	AM	492 738 A	30.06.70	CH				
	AN	16 93 219 A	17.09.70	DE (Abstract)				

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<i>AO</i>	35 12 781 A1	10.04.85	DE (and English language U.S. Patent No. 4,952,740)				
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<i>AQ</i>	97/03679 A	06.02.97	WO				
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BK	Neidlein, et al., "Mild Preparation of 1-Benzoyloxyiminoalkylphosphonic Dichlorides: Application to the Synthesis of Cyclic Phosphonic Diesters and Cyclic Monoester Amides," <u>Heterocycles</u> 35: 1185-1203 (1993)

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BL	Nifant'ev, et al., "1,3,2, - Diazaphosphorinanes", <u>Zh. Obshch. Khim.</u> , Vol. 49, No. 1, 1979, Pages 64-74 (and English version as translated in corresponding English language publication)
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BQ	Shih, et al., "Preparation and Structures of 2-Dimethylamino-4-phenyl-1,3,2-dioxaphosphorinane-2-oxides," <u>Bull. Inst. Chem. Acad. Sin.</u> 41: 9-16 (1994)
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BT	Zon, et al., "4 Cyclophosphamide Analogues," <u>Prog. Med. Chem.</u> 19: 205-246 (1982)

All duplicates

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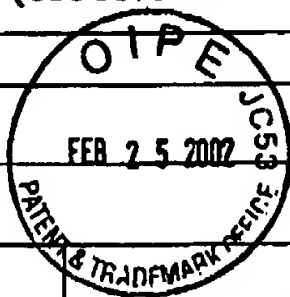
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<b>FORM PTO-1449</b>		<b>ATTY. DOCKET NO.</b> 30727.001	<b>SERIAL NO.</b> 09/518,501
<b>LIST OF PATENTS AND OTHER ITEMS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT</b>  <i>HU</i> (Use several sheets if necessary)		<b>APPLICANT:</b> METABASIS THERAPEUTICS, INC.	
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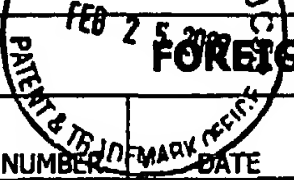
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U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE
<i>TUM</i>	AA	3,018,302	01/23/62	Bielefeld, et al.	260	461	—
<i>TUM</i>	AB	5,157,027	10/20/92	Biller, et al.	514	167	—
<i>TUM</i>	AC	5,658,889	8/19/97	Gruber, et al.	514	43	—

FOREIGN PATENT DOCUMENTS								
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
							YES	NO
<i>TUM</i>	AD	0 002 062 A1	30.05.79	EP (and English language Abstract)				
<i>TUM</i>	AE	0 072 531 A1	23.02.83	EP (and English language Abstract)				
<i>TUM</i>	AF	0 158 057 A	16.10.85	EP (U.K. English language translation)				
	AG	0 180 276 A1	28.12.88	EP				
	AH	0 261 283 A1	22.09.86	EP				
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	AJ	0 338 372 A2	25.10.89	EPO				
	AK	0 353 692 A2	07.02.90	EPO				
	AL	0 481 214 B1	22.04.92	EPO				
	AM	492 738	30.06.70	CH (and English language Abstract)				
<i>✓</i>	AN	987,378	17.09.70	UK				

<b>EXAMINER:</b> <i>James M. Chis</i>	<b>DATE CONSIDERED:</b> <i>7/8/02</i>
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	<b>APPLICANT:</b> METABASIS THERAPEUTICS, INC.	
	<b>FILING DATE:</b> March 5, 1999	<b>GROUP:</b> 1614

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION YES NO
<i>mu</i>	AO	35 12 781 A1	10.04.85	DE (and English language U.S. Patent No. 4,952,740)			
	AP	96/01267	18.01.96	WO			
	AQ	97/03679	06.02.97	WO			
	AR	98/09668	12.03.98	WO			
	AS	98/39342	11.09.98	WO			
	AT	98/39343	11.09.98	WO			
<i>V</i>	AU	98/39344	11.09.98	WO			

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<i>mu</i>	AV	"Patent Abstracts of Japan," Vol. 1998, No. 1, 30 January 1998 & JP 09241284 A (Yamishata Koji, et al.; Nippon Soda Co. Ltd), 16 September 1997
	AW	DeLombaert, et al., "N-Phosphonomethyl Dipeptides and Their Phosphonate Prodrugs, a New Generation of Neutral Endoprptidase (NEP, EC 3.4.24.11) Inhibitors, <u>J. Med. Chem.</u> 37: 498-511 (1994)
	AX	Edmunson, et al., "Cyclic Organophosphorus Compounds. Part 23. Configurational Assignments in the 4-Phenyl-1,3,2λ5-dioxaphosphorinane Series. X-Ray Molecular Structure of <i>cis</i> -2-Benzylamino-4-phenyl-1,3,2-dioxaphosphorinane 2-Oxide," <u>J. Chem. Res. Synop.</u> , 5: 122-123 (1989)
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<i>V</i>	AZ	Farquhar, et al., "Biologically Reversible Phosphate-Protective Groups," <u>J. Pharm. Sci.</u> 72(3): 324-325 (1983)

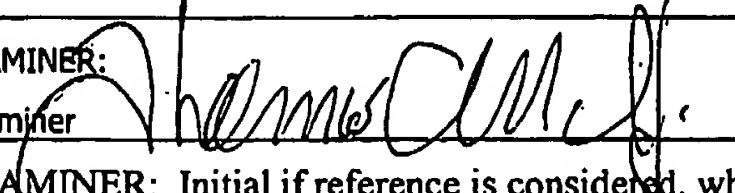
<b>EXAMINER:</b> Examiner <i>Thomas M. Mc...</i>	<b>DATE CONSIDERED:</b> <i>7/9/02</i>
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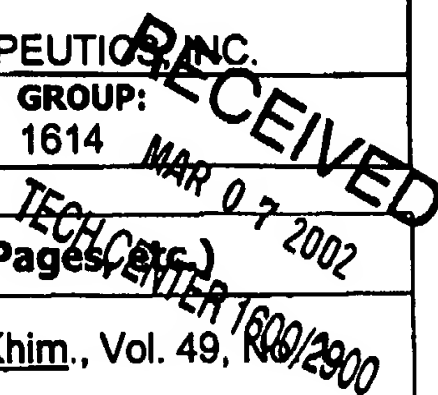
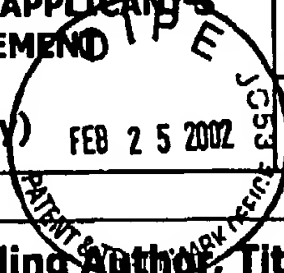
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc)		
✓	BA	Farquhar, et al., "Synthesis and Biological Evaluation of 9-[5'-(2-Oxo-1,3,2-oxazaphosphorinan-2-yl)-β-D-arabinosyl]adenine and 9-[5'-(2-Oxo-1,3,2-dioxazaphosphorinan-2-yl)-β-D-arabinosyl]adenine: Potential Neutral Precursors of 9-[β-D-Arabinofuranosyl]adenine 5'-Monophosphate," <u>J. Med. Chem.</u> 28: 1358-1361 (1985)
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of

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Application Number 09/518,501  
Filing Date March 3, 2000  
First Named Inventor Erlon  
Group Art Unit 1624  
Examiner Name T. McKenzie  
Attorney Docket Number 030727.0013.CIP1

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## U.S. PATENT DOCUMENTS

Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			

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		Office <sup>4</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)				

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AA	Coppi, et al., "Lewis Acid Mediated Condensation of Alkenols and Aldehydes. A Selective Synthesis of Tetrahydropyrans and Oxepanes," J. Org. Chem., Vol. 53, No. 4, 911-913 (1988)	
	AB	Lohr et al., "Targeted chemotherapy by intratumor injection of encapsulated cells engineered to produce CYP2B1, and ifosfamide activating cytochrome P450," Gene Therapy, 5, 1070-1078 (1988).	
	AC	Bijsterbosch, et al., "Disposition of the Acyclic Nucleoside Phosphonate (S)-9-(3-Hydroxy-2-Phosphonylmethoxypropyl)Adenine," Antimicrobial Agents and Chemotherapy, Vol. 42, p. 1146-1150 (May 1998).	
	AD	de Waziers, et al., "Cytochrome P 450 Isoenzymes, Epoxide Hydrolase and Glutathione Transferases in Rat and Human Hepatic and Extrahepatic Tissues1," The Journal of Pharmacology and Experimental Therapeutics, Vol. 253, No.1, p. 387-394 (1989).	

Examiner Signature

Date Considered

2/12/03

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Substitute for form 1449A/PTO			Complete If Known		
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)			Application Number	09/518,501	
			Filing Date	March 3, 2000	
			First Named Inventor	Erion et al.	
			Group Art Unit	1624	
			Examiner Name	McKenzie, T.	
Sheet	1	of	1	Attorney Docket Number	45198.00013.RCE (CIP1)

U.S. PATENT DOCUMENTS						
Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
JL		6,054,587		Reddy et al.	04/25/00	
		6,110,903		Kasibhatla et al.	08/29/00	
		6,284,748		Dang et al.	09/04/01	
		6,294,672		Reddy et al.	09/25/01	
		6,312,662		Erion et al.	11/06/01	
		6,399,782		Kasibhatla et al.	06/04/02	
		6,489,476		Dang et al.	12/03/02	

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Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)				

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Examiner Signature	<i>Tom McKen</i>	Date Considered	4/16/04
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Sheet

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of

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**Complete If Known**

<b>Application Number</b>	<b>09/518,501</b>
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<b>Filing Date</b>	<b>March 3, 2000</b>
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First Named Inventor	Erion et al.
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Group Art Unit	1624
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Examiner Name	T. McKenzie
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Attorney Docket Number	45198.00013.RCE
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## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

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		FARQUHAR et al., "Synthesis and Antitumor Evaluation of Bis[pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <u>J. Med. Chem.</u> , 37:3902-3909 (1994).	
		LEFEBVRE, et al., Mononucleotide Phosphotriester Derivatives with S-Acyl-2-thioethyl Bioreversible Phosphate-Protecting Groups: Intracellular Delivery of 3'-Azido-2',3'-dideoxythymidine 5'-Monophosphate," <u>J. Med. Chem.</u> , 38:3941-3950 (1995).	

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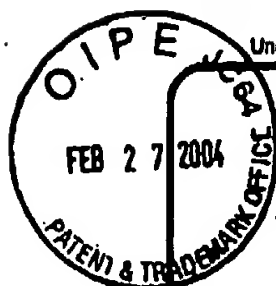
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Sheet 1 of 3

### Complete if Known

Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erion et al.
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	032465.00013.RCE (CIP1)

### U.S. PATENT DOCUMENTS

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)				

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g		Beaucage and Iyer, "The Synthesis of Modified Oligonucleotides by the Phosphoramidite Approach and Their Applications," <u>Tetrahedron</u> , 49(28):6123-6194 (1993).	
		Borch and Millard, "The Mechanism of Activation of 4-Hydroxycyclophosphamide," <u>J. Med. Chem.</u> , 30:427-431 (1987).	
		Cooper et al., "Use of Carbohydrate Derivatives for Studies of Phosphorus Stereo-chemistry. Part II. Synthesis and Configurational Assignments of 1,3,2-Oxathiaphosphorinan-2-ones and 1,3,2-Dioxaphosphorinan-2-thiones," <u>J. Chem. Soc., Perk. Trans. 1</u> , (10):1049-1052 (1974).	
		De Clercq et al., "A Novel Selective Broad-spectrum Anti-DNA Virus Agent," <u>Nature</u> , 323:464-467 (1986).	
		Farquhar et al., "Synthesis and Antitumor Evaluation of Bis[(pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <u>J. Med. Chem.</u> , 37:3902-3909 (1994).	

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erlon et al.
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	032465.00013.RCE (CIP1)

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J		Friis and Bundgaard, "Prodrugs of Phosphates and Phosphonates: Novel Lipophilic $\alpha$ -acyloxyalkyl Ester Derivatives of Phosphate- or Phosphonate Containing Drugs Masking the Negative Charges of these Groups," <u>Euro. J. Pharm. Sci.</u> , 4:49-59 (1996).	
		Harada et al., "Resolution of 1,3-alkanediols Via Chiral Spiroketal Derived from <i>l</i> -Menthone," <u>Tetrahedron</u> , 28(41):4843-4846 (1987).	
		Khorana et al., "Cyclic Phosphates. III. Some General Observations on the Formation and Properties of Five-, Six- and Seven-membered Cyclic Phosphate Esters," <u>JACS</u> , 79:430-436 (1957).	
		Korba et al., "Liver-targeted Antiviral Nucleosides: Enhanced Antiviral Activity of Phosphatidyl-dideoxyguanosine Versus Dideoxyguanosine in Woodchuck Hepatitis Virus Infection <i>In Vivo</i> ," <u>Hepatology</u> , 23(5):958-963 (1996).	
		Lefebvre et al., "Mononucleoside Phosphotriester Derivatives with <i>S</i> -acyl-2-thioethyl Bioreversible Phosphate-protecting Groups: Intracellular Delivery of 3'-azido-2',3'-dideoxythymidine 5'-monophosphate," <u>J. Med. Chem.</u> , 38:3941-3950 (1995).	
		Ludeman et al., "Synthesis and Antitumor Activity of Cyclophosphamide Analogues. 4. Preparation, Kinetic Studies, and Anticancer Screening of "Phenylketophosphamide" and Similar Compounds Related to the Cyclophosphamide Metabolite Aldophosphamide," <u>J. Med. Chem.</u> , 29:716-727 (1986).	
		McGuigan et al., "Intracellular Delivery of Bioactive AZT Nucleotides by Aryl Phosphate Derivatives of AZT," <u>J. Med. Chem.</u> , 36:1048-1052 (1993).	
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		Ramachandran et al., "Efficient General Synthesis of 1,2- and 1,3-diols in High Enantiomeric Excess via the Intramolecular Asymmetric Reduction of the Corresponding Ketoalkyl Diisopinocampheylborinate Intermediates," <u>Tetrahedron</u> , 38(5):761-764 (1997).	

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Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erion et al.
Group Art Unit	1624
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J		Starrett, Jr. et al., "Synthesis, Oral Bioavailability Determination, and <i>in Vitro</i> Evaluation of Prodrugs of the Antiviral Agent 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA)," <u>J. Med. Chem.</u> , 37:1857-1864 (1994).	
		Thomson et al., "Synthesis, Bioactivation and Anti-HIV Activity of the Bis(4-acyloxybenzyl) and Mono(4-acyloxybenzyl) Esters of the 5'-monophosphate of AZT," <u>J. Chem. Soc., Perk. Trans. 1</u> , (11):1239-1245 (1993).	
		Weber and Waxman, "Activation of the Anti-cancer Drug Ifosfamide by Rat Liver Microsomal P450 Enzymes," <u>Biochem. Pharm.</u> , 45(8):1685-1694 (1993).	
		Zon et al., "NMR Spectroscopic Studies of Intermediary Metabolites of Cyclophosphamide. A Comprehensive Kinetic Analysis of the Interconversion of <i>cis</i> - and <i>trans</i> -4-Hydroxycyclophosphamide with Aldophosphamide and Concomitant Partitioning of Aldophosphamide Between Irreversible Fragmentation and Reversible Conjugation Pathways," <u>J. Med. Chem.</u> 27:466-485 (1984).	

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